YELLOW FEVER

DISEASE REPORTING

In Washington

No cases of yellow fever have been reported in Washington in over 50 years.

Purpose of reporting and surveillance

- To identify rare diseases associated with travel.

Reporting requirements

- Health care providers: **immediately notifiable**
- Hospitals: **immediately notifiable**
- Laboratories: notifiable within 2 workdays; specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages.

Laboratory criteria for diagnosis

- Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded, or
- Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

Case definition

- Probable: a clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., ≥ 32 by complement fixation, ≥ 256 by immunofluorescence assay, ≥ 320 by hemagglutination inhibition, ≥ 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme

immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)
- Confirmed: a clinically compatible case that is laboratory confirmed.

A. DESCRIPTION

1. Identification

An acute infectious viral disease of short duration and varying severity. The mildest cases may be clinically indeterminate; typical attacks are characterized by sudden onset, fever, chills, headache, backache, generalized muscle pain, prostration, nausea and vomiting. The pulse may be slow and weak out of proportion to the elevated temperature (the Faget sign). Jaundice is moderate early in the disease and is intensified later. Albuminuria, sometimes pronounced, and anuria may occur. Leukopenia appears early and is most pronounced about the fifth day. Most infections resolve at this stage. After a brief remission of hours to a day, some cases progress into the ominous stage of intoxication manifested by hemorrhagic symptoms including epistaxis, gingival bleeding, hematemesis (coffee-ground or black), melena, and liver and renal failure; 20%-50% of jaundiced cases are fatal. The overall case-fatality rate among indigenous populations in endemic regions is 5% but may reach 20%-40% in individual outbreaks.

Laboratory diagnosis is made by isolation of virus from blood by inoculation of suckling mice, mosquitoes or cell cultures (especially those of mosquito cells); by demonstration of viral antigen in the blood by ELISA or liver tissue by use of labeled specific antibodies; and by demonstration of viral genome in blood and liver tissue by PCR or hybridization probes. Serologic diagnosis is made by demonstrating specific immunoglobulin M (IgM) in early sera or a rise in titer of specific antibodies in paired acute and convalescent sera. Serologic cross-reactions occur with other flaviviruses. Recent infections can often be distinguished from vaccine immunity by complement fixation testing. The diagnosis is supported by demonstration of typical lesions in the liver.

2. Infectious Agent

The virus of yellow fever, of the genus Flavivirus and family Flaviviridae.

3. Worldwide Occurrence

Yellow fever exists in nature in two transmission cycles, a sylvatic or jungle cycle that involves mosquitoes and nonhuman primates, and an urban cycle involving *Aedes aegypti* mosquitoes and humans. Sylvatic transmission is restricted to tropical regions of Africa and Latin America, where a few hundred cases occur annually, most frequently among young adult males who are occupationally exposed in forested or transitional areas of Bolivia, Brazil, Colombia, Ecuador and Peru (with 70%-90% of cases reported from Bolivia and Peru). Historically, urban yellow fever occurred in many cities of the Americas. With the exception of a few cases in Trinidad in 1954, no outbreak of urban yellow fever had been

transmitted by *Ae. aegypti* in the Americas since 1942. However, reinfestation in many cities with *Ae. aegypti* places them at risk of renewed urban yellow fever transmission. In Africa, the endemic zone includes the area between 15N and 10S latitude, extending from the Sahara desert south through northern Angola, Zaire and Tanzania. For the past several decades yellow fever due to *Ae. aegypti* mosquitoes was reported only from Nigeria with nearly 20,000 cases and more than 4,000 deaths between 1986 and 1991. There is no evidence that yellow fever has ever been present in Asia or on the easternmost coast of Africa, although sylvatic yellow fever was reported in 1992-1993 in western Kenya.

4. Reservoir

In urban areas, humans and *Aedes aegypti* mosquitoes; in forest areas, vertebrates other than humans, mainly monkeys and possibly marsupials, and forest mosquitoes. Transovarian transmission in mosquitoes may contribute to maintenance of infection. Humans have no essential role in transmission of jungle yellow fever or in maintaining the virus, but are the primary amplifying host in the urban cycle.

5. Mode of Transmission

In urban and certain rural areas, by the bite of infective *Ae. aegypti* mosquitoes. In forests of South America, by the bite of several species of forest mosquitoes of the genus *Haemagogus*. In east Africa, *Ae. africanus* is the vector in the monkey population, while semidomestic *Ae. bromeliae* and *Ae. simpsoni*, and probably other Aedes species, transmit the virus from monkeys to humans. In large epidemics in Ethiopia, good epidemiologic evidence incriminated *Ae. simpsoni* as a person to person vector. In west Africa, *Ae. furcifer-taylori*, *Ae. luteocephalus* and other species are responsible for spread between monkeys and humans. *Ae. albopictus* has been introduced into Brazil and the US from Asia and has the potential for bridging the sylvatic and urban cycles of yellow fever in the Western Hemisphere. However, no instance of involvement of this species in yellow fever transmission has been documented.

6. Incubation period

Three to six days.

7. Period of communicability

Blood of patients is infective for mosquitoes shortly before onset of fever and for the first 3-5 days of illness. The disease is highly communicable where many susceptible people and abundant vector mosquitoes coexist; not communicable by contact or common vehicles. The extrinsic incubation period in *Ae. aegypti* is commonly 9-12 days at the usual tropical temperatures. Once infected, mosquitoes remain so for life.

8. Susceptibility and resistance

Recovery from yellow fever is followed by lasting immunity; second attacks are unknown. Mild inapparent infections are common in endemic areas. Transient passive immunity in infants born to immune mothers may persist for up to 6 months. In natural infections, antibodies appear in the blood within the first week.

B. METHODS OF CONTROL

1. Preventive measures:

a. Institute a program for active immunization of all people 9 months of age or older necessarily exposed to infection because of residence, occupation or travel. A single subcutaneous injection of a vaccine containing viable attenuated yellow fever 17D strain virus, cultivated in chick embryo, is effective in almost 99% of recipients. Antibodies appear 7-10 days after immunization and may persist for at least 30-35 years, probably much longer, though immunization or reimmunization within 10 years is required by the International Health Regulations for travel from endemic areas.

   Since 1989, WHO has recommended that at-risk countries in Africa that fall in the endemic-epidemic belt should incorporate yellow fever vaccine into their routine childhood immunization programs. As of March 1998, there were 17 African countries with such a policy but, only two that have achieved 50% coverage. The vaccine can be given any time after 6 months of age and can be administered with other antigens such as measles vaccine.

   The vaccine is contraindicated in the first 4 months of life and should be considered for those aged 4-9 months only if the risk of exposure is judged to exceed the risk of vaccine-associated encephalitis, the principal complication in this age group. The vaccine is also not recommended in circumstances where live virus vaccines are contraindicated, nor in the first trimester of pregnancy, unless the risk of disease is believed to be higher than the theoretical risk to the pregnancy. There is, however, no evidence of fetal damage from the vaccine, but lower rates of maternal seroconversion have been observed, an indication for reimmunization after termination of the pregnancy. The vaccine is recommended for asymptomatic HIV seropositive individuals; there is insufficient evidence to permit a definitive statement on whether the vaccine would pose a risk for symptomatic individuals.

b. For urban yellow fever eradicate or control of *Ae. aegypti* mosquitoes; immunization when indicated.

c. Sylvan or jungle yellow fever, transmitted by Haemagogus and forest species of Aedes, is best controlled by immunization, which is recommended for all people in rural communities whose occupation brings them into forests in yellow fever areas, and for people who intend to visit those areas. Protective clothing, bed nets and repellents are advised for those not immunized.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Blood and body fluid precautions. Prevent access of mosquitoes to patient for at least 5 days after onset by screening the sickroom, by spraying quarters with residual insecticide, and by using a bed net.
c. Concurrent disinfection: None; the home of patients and all houses in the vicinity should be sprayed promptly with an effective insecticide.
d. Quarantine: None.
e. Immunization of contacts: Family and other contacts and neighbors not previously immunized should be immunized promptly.
f. Investigation of contacts and source of infection: Inquire about all places, including forested areas, visited by the patient 3-6 days before onset, to locate focus of yellow fever; observe all people visiting that focus. Search premises, and places of the patient's work or visits over the preceding several days for mosquitoes capable of transmitting infection; eradicate them with effective insecticide. Investigate mild febrile illnesses and unexplained deaths suggesting yellow fever.
g. Specific treatment: None.

3. Epidemic measures

a. Urban or *Ae. aegypti* transmitted yellow fever:
    i. Mass immunization, beginning with people most exposed and those living in *Ae. aegypti* infected areas.
    ii. Spraying the inside of all houses in the community with insecticides has shown promise for controlling urban epidemics.
    iii. Eliminate or apply larvicide to all actual and potential breeding places of *Ae. aegypti*.
b. Jungle or sylvan yellow fever:
    i. Immediately immunize all people living in or near forested areas or entering such areas.
    ii. Ensure that nonimmunized individuals avoid those tracts of forest where infection has been localized, and that those just immunized avoid the areas for the first week after immunization.
c. In regions where yellow fever may occur, a diagnostic viscerotomy service should be organized to collect small specimens of liver post mortem from fatal febrile illnesses of 10 days duration or less; facilities for viral isolation or serologic confirmation are necessary to establish the diagnosis since histopathologic changes in the liver are not pathognomonic of yellow fever.
d. In Central and South America, confirmed deaths of howler and spider monkeys in the forest are presumptive evidence of the presence of yellow fever. Confirmation by the histopathologic examination of livers of moribund or recently dead monkeys or by virus isolation is highly desirable.
e. Immunity surveys by neutralization tests of wild primates captured in forested areas are useful in defining enzootic areas. Serologic surveys of human populations are almost useless where yellow fever vaccine has been widely used.

4. International measures

a. Telegraphic notification by governments to WHO and to adjacent countries of the first imported, first transferred, or first nonimported case of yellow fever in an area previously free of the disease; and of newly discovered or reactivated foci of yellow fever infection among vertebrates other than man.
b. Measures applicable to ships, aircraft and land transport arriving from yellow fever areas are specified in the International Health Regulations (1969), Third Annotated Edition 1983, Updated and Reprinted 1992, WHO, Geneva. These regulations are being revised, but the new regulations are not expected to be available until sometimes in the year 2002 or after.
c. Animal quarantine: Quarantine of monkeys and other wild primates arriving from yellow fever areas may be required until 7 days have elapsed after leaving such areas.
d. International travel: A valid international certificate of immunization against yellow fever is required by many countries for entry of travelers coming from or going to recognized yellow fever zones of Africa and South America; otherwise, quarantine measures are applicable for up to 6 days. Immunization is recommended by WHO for all travelers to areas other than major cities in countries where the disease occurs in humans or is assumed to be present in nonhuman primates. The International Certificate of Vaccination against Yellow Fever is valid from 10 days after date of immunization for 10 years; if reimmunized within that period, valid from date of reimmunization for 10 years.